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Brief Clinical Report

XX-Agonadism in a Fetus With Multiple Dysraphic Lesions: A New Syndrome

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We report on a 19-week-old fetus with a 46,XX karyotype, normal female external genitalia, complete gonadal agenesis, large encephalocele, spina bifida, and omphalocele. We postulate a new syndrome. Hitherto no consistent malformation patterns have been observed in agonadism patients. True agonadism, including even the unusual finding of an XX gonosomal status, is obviously not as rare as suggested. Am. J. Med. Genet. 70:413–414, 1997. © 1997 Wiley-Liss, Inc.

KEY WORDS: agonadism; associated malformations

INTRODUCTION

Earlier reports suggest that agonadism is a rare, non-familial condition, mostly without associated malformations, and almost always consistent with a 46,XY karyotype [Kennerknecht et al., 1995]. An increasing number of reports shows agonadism associated with malformations and an XX gonosomal status. This is the fifth report of XX-agonadism including four sporadic cases: three without [Levinson et al., 1976, n = 1; Medina et al., 1982, n = 2] and one with associated malformations [this report], and two familial observations. The latter two reported agonadal sisters with XX and XY sex chromosomes, respectively, one pair without [Mendonça et al., 1994] and the other pair with extragenital malformations [Kennerknecht et al., 1993]. Since three of these six observations were ascertained by us without a systematic search, 46,XX agonadism may not be as rare as suggested previously but rather seems to have been overlooked.

CLINICAL REPORT

The patient was ascertained in the ninth week of gestation during routine ultrasound scan. An encephalocele of the left hemisphere and ventricle and severe thoracal and spinal malformations were detected. Cytogenetic studies showed a normal female karyotype 46,XX in chorionic villus short-term culture and in amniotic fluid cell culture. Twenty-five to thirty metaphases were analyzed from each culture using QFQ-banding technique at least at an 550 band level except for CVS. The pregnancy was terminated because of the malformations.

Pathological examination showed a large encephalocele that extended from the occipital region to the upper third of the spine. Below the cele, a dysraphic segment of the spine (spina bifida) of 45 mm length was found. On the ventral aspect of the body an omphalocele could be demonstrated that enclosed parts of the gut and of the omentum. Despite careful search, no gonads or internal genital organs could be detected.

The family history was unremarkable. The parents are not consanguineous. At the time of interruption the mother was 32 and the father 30 years old. This was their second pregnancy. In a previous partnership the mother experienced a spontaneous abortion in the second month of gestation. The reason was unknown and no further information were available.

DISCUSSION

True agonadism is thought to be rare, mostly sporadic with XY sex chromosomes, and without extragenital anomalies. The fact that we have had two familial observations and one isolated case suggests that cases are being overlooked or not reported. The malformation pattern of the present case is again unique and presents a newly recognized syndrome clearly distinct from other reports [Sarto and Opitz, 1973; Carey et al., 1978; Opitz and Gilbert, 1982; Carmi et al., 1990; Ma-

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ciel-Guerra et al., 1991; Meacham et al., 1991; Kushnik et al., 1992; Maaswinkel-Mooij and Stokvis-Brantsma, 1992; Kennerknecht et al., 1993, 1995; Sybert et al., 1995].

The pathogenetic considerations of XX-agonadism was discussed by Kennerknecht et al. [1993, 1995]. None of these observations allows differentiation between agonadism (i.e., primary absence of gonads) or secondary regressions of gonadal structures. The type of associated malformations, such as multiple dysraphic lesions [this report] or multiple mesodermal midline defects [Kennerknecht et al., 1993] both covering several neighbouring developmental fields, suggests abnormal expression of a developmental gene (e.g., homeobox genes) in early embryogenesis. Yet, the time pattern is still unclear.

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